ATTORNEY'S DOCKET NUMBER: U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE BO 43339 TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) USIAQLININGRIF ROWNS = 7378F = 25) CONCERNING A FILING UNDER 35 U.S.C. 371 PRIORITY DATE CLAIMED: INTERNATIONAL FILING DATE: INTERNATIONAL APPLICATION NO.: 7 FEBRUARY 2000 5 FEBRUARY 1999 PCT/NL00/00075 TITLE OF INVENTION: METHOD OF MODULATING METABOLITE BIOSYNTHESIS IN RECOMBINANT CELLS APPLICANT(S) FOR DO/EO/US: Johan MEMELINK, Cornelia Theodora Elisabeth VAN DER FITS, Franciscus Leonardus Hendrikus MENKE and Jan Willem KIJNE Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information: This is a FIRST submission of items concerning a filing under 35 U.S.C. 371. 1. This is a SECOND or SUBSEQUENT submission of items concerning a filing under 35 U.S.C. 371. 2. This express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration Х 3 of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1). A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date. Х 4. A copy of the International Application as filed (35 U.S.C. 371(c)(2)) 5. ıĒ is transmitted herewith (required only if not transmitted by the International Bureau). a. has been transmitted by the International Bureau. (see attached copy of PCT/IB/308) b. ŭ U is not required, as the application was filed in the United States Receiving Office (RO/US). C. A translation of the International Application into English (35 U.S.C. 371(c)(2)). 6. Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3)). are transmitted herewith (required only if not transmitted by the International Bureau). a. have been transmitted by the International Bureau. b. have not been made; however, the time limit for making such amendments has NOT expired. C. d. have not been made and will not be made. A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)). 8.3 An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)). 9. A translation of the annexes of the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)). 10. Item 11. to 16. below concern document(s) or information included: An Information Disclosure Statement under 37 CFR 1.97 and 1.98. 11. An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included. 12. A FIRST preliminary amendment. Х 13. A SECOND or SUBSEQUENT preliminary amendment. 14. A substitute specification. A change of power of attorney and/or address letter. 15. 16. Other items or information: INTERNATIONAL PRELIMINARY EXAMINATION REPORT (PCT/IPEA/409), INTERNATIONAL SEARCH

REPORT (PCT/ISA/210), Form PCT/IB/304, SUBMISSION UNDER 37 CFR §821 FOR PATENT APPLICATIONS CONTAINING SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES, SEQUENCE LISING ON PAPER AND DISKETTE, ABSTRACT OF THE DISCLOSURE on a separate sheet, and APPLICATION DATA SHEET

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S: APPLICATION NO.	Sam, see 37 CFR 1.5)	INTERNATIONAL APPLIC	CATION NO.		ATTORNEY'S DOCKET NO. BO 43339	
				CALCULATIONS PTO USE ONLY		
17. X The following fees are submitted:					-	
BASIC NATIONAL FEE (37 CFR 1.492(a)(1)-(5)):						
Neither international preliminary examination fee (37 CFR1.482) nor international search fee (37 CFR1.445(a)(2)) paid to USPTO and International Search Report not prepared by the EPO or JPO						
International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO						
International preliminary examination fee (37 CFR 1.482) not paid to USPTO but international search fee (37 CFR 1.445(a)(2)) paid to USPTO						
International preliminary examination fee (37 CFR 1.482) paid to USPTO but all claims did not satisfy provisions of PCT Article 33(1)-(4)						
International preliminary examination fee (37 CFR 1.482) paid to USPTO and all claims satisfied provisions of PCT Article 33(1)-(4)						
ENTER APPROPRIATE BASIC FEE AMOUNT =				\$	860.00	
Surcharge of \$130.00 for furnishing the oath or declaration later than 30 months from the earliest claimed prior (\$37 CFR 1.492(e)).				\$	130.00	
CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE	\$	_	
Total-claims	24 - 20 =	4	X \$18.00	\$	72.00	
Independent claims	4 - 3 =	1	X \$80.00	\$	80.00	
MULTIPLE DEPENDENT CLAIMS(S) (if applicable) +\$270.00				\$		
TOTAL OF ABOVE CALCULATIONS =				\$	1,142.00	
Reduction of ½, if applicant is entitled to Small Entity status under 37 CFR 1.27.				\$	<u> </u>	
SUBTOTAL =				\$	1,142.00	"…
Processing fee of \$130 for furnishing the English translation later than months from the earliest claimed priority date (37 CFR1.49(f)).				\$		
TOTAL NATIONAL FEE =				\$	1,142.00	
Fee for recording the enclosed assignment (37 CFR1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). \$40.00 per property				\$		*
TOTAL FEES ENCLOSED =				\$	1,142.00	
				Amount to be		
				refunded: charged:		
a. X A check in the amount of \$ 1,142.00 to cover the above fees is enclosed.						
b. Please charge my Deposit Account No. 25-0120 in the amount of \$ to cover the above fees. A duplicate copy of this sheet is enclosed.						
c. X The Commissioner is hereby authorized to charge any additional fees which may be required by 37 CFR 1.16 and 1.17, or credit any overpayment to						
Deposit Account No. 25-0120. A duplicate copy of this sheet is enclosed.						
SEND ALL CORRESPONDENCE TO:					Castel	
CUSTOMER No. 00466 By				, Jews		
Young & Thompson 745 South 23rd Street		August 6, 2001	Benoît Castel Attorney for Applicants			
				egistration	No. 35,041	
(703) 521-2297					•	
facsimile (703) 685-057	73					